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09/553,431	04/19/00	OSTERYOUNG	K 920905.90041

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EXAMINER

KUBELIK, A

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/553,431	Applicant(s) OSTERYOUNG, KATHERINE W.
	Examiner Anne Kubelik	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 19 April 2000.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 9 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-8 and 10-28 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) Notice of References Cited (PTO-892)
- 16) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 18) Interview Summary (PTO-413) Paper No(s). _____.
- 19) Notice of Informal Patent Application (PTO-152)
- 20) Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-8 and 10-28, drawn to a nucleic acid of SEQ ID NO:1, transgenic plants comprising that nucleic acid, and a method of using that nucleic acid to alter the size, shape and number of plastids in a plant cell, classified in class 800, subclass 278, for example.
 - II. Claims 1-7 and 9-28, drawn to a nucleic acid of SEQ ID NO:3, transgenic plants comprising that nucleic acid, and a method of using that nucleic acid to alter the size, shape and number of plastids in a plant cell, classified in class 536, subclass 23.6, for example.

Claims 1-7 and 10-28 will be examined to the extent they read on the elected invention.

The inventions are distinct, each from the other, because:

Inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation. Applicant is reminded that nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute **independent and distinct** inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. This requirement is

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not to be construed as a requirement for an election of species, since each nucleotide and amino acid sequence is not a member of single genus of invention, but constitutes an independent and patentably distinct invention. Additionally, a search on more than one sequence is a severe burden on PTO resources.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, fields of search, and classification, restriction for examination purposes as indicated is proper.

During a telephone conversation with Nicholas Seay on 21 May, 2001, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-8 and 10-28 to the extent they read on SEQ ID NO:1. Affirmation of this election must be made by Applicant in replying to this Office action. Claim 9 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

2. Claims 1 and 14 are objected to because "cause" in lines 6 and 12, respectively, should be "causes". Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to a DNA sequence comprising SEQ ID NO:1, which reads on a product of nature.

The DNA molecule, as claimed, has the same characteristics and utility as those found naturally in the genome or as cellular precursors thereof and therefore does not constitute patentable subject matter. See *American Wood v. Fiber Disintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). It is suggested that the claim be modified to refer to the hand of the inventor, e.g. by replacing "A" with --An isolated-- or --A purified--.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 4, 7, 10-12, 14, 17, 20, 23-24 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an *Arabidopsis MinD* gene encoding SEQ ID NO:2, plants transformed with that gene, and methods of using that gene to alter size, shape and/or number of plastids, does not reasonably provide enablement for any *MinD* coding sequence from any source, plants transformed with any *MinD* coding sequence, or methods of using any *MinD* coding sequence to alter size, shape and/or number of plastids. The specification does not enable any person skilled in the art to which it pertains, or with which it is

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most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to plants transformed with any MinD coding sequence, methods of using any MinD coding sequence to alter size, shape and/or number of plastids in any plant, and DNAs encoding any plant MinD protein.

The instant specification, however, only provides guidance for a MinD sequence from *Arabidopsis*, its use to alter size, shape and/or number of plastids in *Arabidopsis*, and *Arabidopsis* plants transformed with the *Arabidopsis* MinD coding sequence in a sense or antisense orientation. No guidance is provided for use of any MinD sequence from any source, for plants having altered size, shape and/or number of plastids as a result of transformation with any MinD coding sequence, or for a MinD coding sequence from any source.

Additionally, the instant specification, however, fails to provide guidance for plant MinD sequences other than those from *Arabidopsis* or *Tagetes*. It fails to provide guidance for which amino acids of those sequences can be altered to which other amino acids, and which amino acids must not be changed, to produce a MinD coding sequence from any plant. The specification also fails to provide guidance for which amino acids can be deleted and which regions of the protein can tolerate insertions and still produce a functional enzyme.

Making these alterations is unpredictable. Making “conservative” substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (*supra*) showed that the “conservative” substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while “nonconservative” substitutions with alanine or asparagine had no effect (abstract).

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Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the “nonconservative” amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the “conservative” amino acid arginine drastically reduced enzyme activity (see Table 1).

Sense and antisense constructs can behave unpredictably when transformed into a heterologous plant species. Sweetlove et al (1996, Biochem. J. 320:493-498) found no differences in starch content, tuber number, tuber weight, or metabolite content between potatoes transformed with a sense *E. coli* ADP-glucose pyrophosphorylase gene and potatoes from control plants, even though the activity of the enzyme was four-fold higher in the transformed plants (pg 495, entire pg, and pg 497, right column, paragraph 3). Colliver et al (1997, Plant Mol. Biol. 35:509-522) showed that transformation of bird’s foot trefoil with a construct that was antisense to bean chalcone synthase unexpectedly resulted in transformants with *increased* levels of chalcone synthase transcripts (pg 519, left column, paragraph 2).

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for using any MinD coding sequence to alter size, shape and/or number of plastids in any plant, plants transformed with any MinD coding sequence, and DNAs encoding any plant MinD protein.

7. Claims 1-7 and 10-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for alteration of size, shape and/or number of plastids in *Arabidopsis* via antisense expression of SEQ ID NO:1, does not reasonably provide enablement

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for alteration of size, shape and/or number of plastids in any plant via antisense expression of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to methods of altering the size, shape and/or number of plastids in plant cells by transformation with an antisense *Arabidopsis* MinD gene construct, plants so obtained, and constructs used in that method. The instant specification, however, fails to provide guidance for the antisense inhibition of MinD genes other than that of *Arabidopsis*.

Constructing an antisense RNA sequence that reliably inhibits gene expression is an unpredictable science. Antisense constructs that are not completely homologous can have very unpredictable effects. As discussed above, Colliver et al (*supra*) showed that transformation of bird's foot trefoil with a construct that was antisense to bean chalcone synthase resulted in transformants with *increased* levels of chalcone synthase transcripts (pg 519, left column, paragraph 2) and note other instances when this phenomenon has occurred (pg 519, right column, paragraph 1).

Plants of different species in which the expression of the same gene is inhibited via antisense constructs can behave very differently. While tomatoes containing an antisense acid invertase DNA construct grew identically to control plants (Klann et al, 1996, Plant Physiol. 112:1321-1330; see the abstract and pg 1323, right column, paragraph 1), carrot development is drastically altered when acid invertase expression is reduced via an antisense construct (Tang et al, 1999, Plant Cell 11:177-189; see pg 179, left column, paragraphs 1-2, and pg 184, left column, paragraph 1).

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As the antisense *Arabidopsis* MinD gene construct was not shown to work in plants other than *Arabidopsis*, the unpredictability of behavior of antisense constructs has not been overcome.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate methods for altering the size, shape and/or number of plastids in plant cells by transformation with an antisense *Arabidopsis* MinD gene construct.

8. Claims 1, 4, 7, 10-12, 14, 17, 20, 23-24 and 27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to plants transformed with a multitude of DNA molecules that encode a MinD protein of any sequence and from any source, methods of using those DNA molecules, and DNA molecules encoding a MinD protein from any plant. In contrast, the specification only describes a coding sequence from *Arabidopsis* that comprises SEQ ID NO:1 or encodes SEQ ID NO:2, a method for its use, and *Arabidopsis* plants transformed with sense and antisense constructs comprising that DNA. No process for obtaining a MinD protein of any sequence and from any source is disclosed, nor are any crucial or characteristic MinD-characteristic sequence motifs disclosed. Hence, Applicant has not, in fact, described a DNA molecule that encodes any MinD protein, and the specification fails to provide an adequate written description of the claimed invention.

See *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism

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and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism that would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-8 and 10-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-8 and 10-28 are indefinite because they include nonelected matter.

Claim 11 is indefinite because it compares a plant having a transgene to another plant having the same transgene. For purposes of examination, it was assumed that the comparison was to a plant that lacked the transgene. Such treatment does not relieve Applicant of the responsibility to respond to this rejection. Dependent claims are included in the rejection.

Claim 27 is indefinite because it is not clear if the phrase "comprising a plant MinD gene" modifies "genome" or "sequence." For purposes of examination, it was assumed that the phrase modified "sequence." Such treatment does not relieve Applicant of the responsibility to respond to this rejection.

11. Claims 24-26 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Method steps must be circular; the final step must generate the item the method is intended to produce. The method of altering the size, shape and/or number of plastids in plant

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cells in claim 24 ends in expression of a gene, when it should end in the production of plant cells with altered size, shape and/or number of plastids. Claims 25-26 are dependent on claim 24; correction of the problem in claim 24 will also correct it in claims 25-26.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 8 and 27-28 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Sato et al (1998, DNA Res. 5:41-54).

Sato et al teach an isolated nucleic acid that is 100% identical to SEQ ID NO:1 and encodes an *Arabidopsis MinD* gene (see sequence search results).

14. Claims 1-7 and 11-26 are free of the prior art, given the failure of the prior art to teach or fairly suggest methods of altering the size, shape and/or number of plastids in plant cells by transformation with a sense or antisense MinD gene, the constructs used in that method, or the plants or seeds so obtained.

Conclusion

15. No claim is allowed.

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16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059.

The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.

June 26, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180-1638

David T. Fox